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10/594,674	02/13/2007	Mohammad Djavad Mossalayi	604-790	2319

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EXAMINER	
HUYNH, PHUONG N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,674	MOSSALAYI ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *15-20, 22-31, 33-34, 37-39, 42-48, 50, 52-55 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,21,32,35,36,40,41,49,51 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 July 2007* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/1/06; 9/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-57 are pending.

2. Applicant's election of Group I (now claims 1-14, 21, 32, 35-36, 38, 40-41, 49, 51 and 56) in the reply filed on May 29, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

   Upon reconsideration, the prior art search has been extended to include peptidomimetic labeled with a detectable marker of claim 49.

3. Claims 15-20, 22-31, 33-34, 37-39, 42-48, 50, 52-55 and 57 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-14, 21, 32, 35-36, 40-41, 49, 51 and 56, drawn to a compound comprising a CD23-binding peptide, an isolated polypeptide an amino acid sequence selected from the group consisting of SEQ ID NO: 1-10, an active fragment thereof, a peptidomimetic thereof other than retroinverted peptide thereof and cyclic peptide thereof, and a pharmaceutical composition comprising said peptide or polypeptide, are being acted upon in this Office Action.

5. Claims 2-9 are objected to because the preamble "The peptide" in claims 2-9 is inconsistent with the preamble "A compound" of claim 1. It is suggested that the preamble of claim 1 be amended to recite "An isolated peptide" to provide antecedent basis for said dependent claims. If claim 1 is amended, Applicant is reminded that the "compound" in claims 13 and 40-41 are also needed to be amended.

6. Claim 38 is objected to under 37 CFR 1.821(d) because SEQ ID NO: is required for the sequence "spwneh". Further, all amino acid residues should be in capital letter.

7. Claim 49 is objected to because the word "labelled" is misspelled.

8. Claim 51 is objected to under 37 CFR 1.821(d) because sequence identifier (SEQ ID NO:) is required for any peptide sequence listed in Table 1 and II of four or more amino acid residues, see MPEP § 2422.01. Further, the plural peptides and peptidomimetics at line 2 are inconsistent with the singular polypeptide or peptidomimetic in line 1 of claim 51. Correction is required. Claim 51 is further objected to for reciting non-elected embodiment.

9. The drawings are objected to because Figure 1 is too dark. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

10. The disclosure is objected to under 37 CFR 1.821(d) because sequence identifier SEQ ID NO: is required for the sequences listed in Table 1 and 2.

11. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: alterations by inventor Christopher R Self which have not been initialed and/or dated as is required by 37 CFR 1.52(c). The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of

which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-14, 21, 32, 35-36, 40-41, 49, 51 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated CD23 binding peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1-10, (2) the said isolated peptide wherein the N-terminus of the peptide is acylated or the C-terminus of the peptide is amidated, (3) the said isolated peptide wherein the peptide is labeled for detection assays, (4) the isolated CD23 binding peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1-10 wherein at least one amino acid within said peptide is a D-isomer, (5) An isolated CD23 binding peptide consisting of the amino acid sequence of SEQ ID NO: 1 for treating rheumatoid arthritis by inhibiting Nitric oxide production and TNF production, **does not** reasonably provide enablement for any compound or peptide or pharmaceutical composition comprising such compound or peptide as set forth in claims 1-14, 21, 32, 35-36, 40-41, 49, 51 and 56 for treatment or prophylaxis of any disease or any disorder related to CD23 such as any autoimmune diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient

to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The claims encompass numerous compounds and polypeptides comprising any CD23-binding peptide comprising any combination of amino acid residues X1, X2, X3, X4, X5, S6, S7 and X8 for preventing any diseases, any autoimmune diseases, or any disorders related to CD23.

Enablement is not commensurate in scope with how to make and use any compound or polypeptide longer than the peptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1-10 for treating or preventing any and all diseases such as any autoimmune diseases.

The specification discloses only peptide consisting of six or seven amino acid residues in length selected from the group consisting of SEQ ID NO: 1-10 or the specific peptide listed in Table I and II that inhibits the binding of monoclonal CD23 antibody to CD23 expressing cell *in vitro*. The specification discloses the N-terminus of the peptide HENWPS (SEQ ID NO: 7) is acylated or the C-terminus of the peptide is amidated. The specification discloses only one retroinverted peptide from HENWPS (SEQ ID NO: 7), which is SPWNEH. However, only the specific peptides of SEQ ID NO: 1-7 inhibit iNOS production as shown in Table 2. The specification further discloses administering only peptide FHENWPS (p30A) of SEQ ID NO: 1 inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (an adjuvant induced model of arthritis).

At the time of invention, the specification does not disclose any compound or polypeptide other than the specific peptides consisting of the amino acid sequence of SEQ ID NO 1-10. There is insufficient guidance as to the structure of any compound or any polypeptide longer than 7 amino acid residues. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends. There is a lack of guidance as to which amino acids to be added such that the peptide still retains binding to CD23. Further, the term "a polypeptide having *an* amino acid sequence" encompasses full length sequence as well as fragment thereof because of the term "an".

With respect to polypeptide comprising the peptide of claim 1 wherein said polypeptide comprises from about 6 to about 100 amino acids (claim 10) or from about 6 to about 70 amino acids (claim 11), there is not a single polypeptide longer than 7 amino acid residues in the specification as filed. As such, the rest of 93 amino acid residues or 63 residues in the polypeptide, respectively, are not enabled.

With respect to any "peptidomimetic", the specification discloses only the peptide of SEQ ID NO: 1 is either D-isomer, the N-terminus of the peptide is either acylated or acetylated or the C-terminus is amidated. The specification does not teach substituting any amino acids, deleting, adding and/or a combination thereof in the peptide of SEQ ID NO: 1 still binds specifically to CD23, other than the ones disclosed in Table I.

The specification at page 8 defines "peptidomimetic" is a compound that mimics the 'biological activity of a peptide but *is no longer peptidic in chemical nature.* A peptidomimetic is a compound that may no longer contain any peptide bonds (that is, amide bonds between amino acids). The term peptidomimetic as used herein includes within its meaning compounds that are no longer completely peptidic in nature, such as pseudo-peptides, semi-peptides and peptoids. Whether completely or partially non-peptide, peptidomimetics according to this invention provide a spatial arrangement of reactive chemical moieties that closely resembles the three-dimensional arrangement of active groups in the peptide on which, the peptidomimetic is based. As a result of this similar active-site geometry, the peptidomimetic has effects on biological systems which are similar to the biological activity of the peptide. The present invention encompasses peptidomimetic compositions which are analogs that mimic the activity of biologically active peptides according to the invention, i.e., the peptidomimetics are capable of binding to CD23.

However, the specification does not provide specific guidance regarding any biological function of any "peptidomimetic" that mimics the 'biological activity of a peptide but *is no longer peptidic in chemical nature* or any *in vivo* working examples for treating or preventing any autoimmune diseases.

It is well known in the prior art that the amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence to obtain a desired biological activity requires knowledge and guidance regarding specific amino acid residue(s) in the protein's amino acid sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification) and detailed knowledge of the protein's structure, and the ways in which the protein's structure relates to its function.

Stryer et al (in Biochemistry, Third edition, W H Freeman Company, New York, pages 31-33, 1998; PTO 892). teach that a protein is highly dependent on the overall structure of the

protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a protein having the same biological activity are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Ngo et al (The Protein Folding Problem and Tertiary Structure Prediction, pp. 491-495, 1994; PTO 892) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 with an expectation of obtaining a derivative maintaining the same biological activity.

At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the specification discloses substituting even a single amino acid in the peptide of SEQ ID NO: 1 from P to A resulted in lost of inhibition of iNOS production from 74% to 26%, see specification at page 28, Table II compound 328, in particular.

With respect the pharmaceutical composition comprising any compound, any polypeptide or any peptidomimetic, the specification discloses administering only one peptide (p30A) consisting of the amino acid sequence FHENWPS (SEQ ID NO: 1) that inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

However, the specification does not disclose administering any compound, any protein comprising any peptide sequence as set forth 1, 10-12, and 21 or any peptidomimetic thereof is effective for treating any diseases, much less preventing any and all diseases, any diseases such as any autoimmune diseases.

Given the enormous number of compounds, polypeptides, and peptidomimetics, there is insufficient *in vivo* working example to show administering one species of peptide (SEQ ID NO: 1) is predictable of treating and preventing all diseases, especially all autoimmune diseases.

Van Noort et al (International Review of Cytology 178: 127-205, 1998; PTO 892) teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular).

Since the therapeutic indices of compound, protein or peptide can be species- and model-dependent, it is not clear that reliance on the use of adjuvant induced arthritis rat model and one peptide consisting with SEQ ID NO: 1 accurately reflects the relative efficacy of treating all diseases by administering all compound, polypeptide or peptidomimetic, much less preventing any and all autoimmune diseases.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

15. Claims 1-14, 21, 32, 35-36, 40-41, 49, 51 and 56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a genus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent.

Claim 2 encompasses a subgenus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein

X_1 is Phe, X_2 is His; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, and X_8 is absent.

Claim 3 encompasses a subgenus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 or SEQ ID NO: 6.

Claim 4 encompasses a genus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is absent, X_2 is His; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn; X_5 is Trp; X_6 is Pro; X_7 is Ser and X_8 is Phe, Gly or is absent.

Claims 5-6 encompass a subgenus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, or SEQ ID NO: 10.

Claims 7-9 encompasses a genus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein the N-terminus is acylated, acetylated or the C terminus is amidated.

Claim 10 is drawn to a genus of polypeptide comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein said polypeptide *comprises* from about 6 to about 100 amino acids in length.

Claim 11 is drawn to a genus of polypeptide comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein said polypeptide *comprises* from about 6 to about 70 amino acids in length.

Claim 12 is drawn to a genus of polypeptide comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein said polypeptide *comprises* from about 6 to about 15 amino acids in length.

Claim 13 is drawn to a genus of compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent having binding to any CD23 of at least about 10^{-6} M.

Claim 14 is drawn to a genus of pharmaceutical composition comprising at least any one compound comprising any CD23-binding peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent and a pharmaceutically acceptable carrier.

Claim 21 is drawn to a genus of isolated polypeptide *comprising* a) any polypeptide *comprising* an amino acid sequence selected from the group consisting of SEQ ID NO: 1-10, b) any polypeptide *comprising* an amino acid sequence at least about 83% identical to any amino acid sequence of SEQ ID NO: 1-10; c) any biologically active fragment of any polypeptide having an amino acid sequence of SEQ ID NO: 1-10; and any immunogenic fragment of any polypeptide having an amino acid sequence of SEQ ID NO: 1-10.

Claim 35 is drawn to a genus of peptidomimetic of any peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent.

Claim 36 is drawn to a genus of peptidomimetic of any peptide *comprising* at least one D-amino acid isomer of an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-

X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent.

Claim 40 is drawn to a genus of peptidomimetic of any peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein the peptidomimetic having a specific binding to any CD23 of at least about 10^{-6} M.

Claim 41 is drawn to a genus of pharmaceutical composition comprising a genus of peptidomimetic of any peptide *comprising* any amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent and a pharmaceutically acceptable carrier.

Claim 49 is drawn to a genus of peptidomimetic of any labeled peptide *comprising* an amino acid sequence with any combination of X_1-X_2X_3-X_4-X_5-X_6-X_7-X_8 wherein X_1 is Phe or is absent, X_2 is His or Ala; X_3 is Glu, Ser, Ala, Asn, Lys, or Cys; X_4 is Asn, Phe, Gln, Pro, Ser, or Ala; X_5 is Trp; X_6 is Pro, Arg, Glu, Gly, Cys, or Lys; X_7 is Ser, Pro, Leu, Thr, Ala, Gly, Asn or absent and X_8 is Phe, Gly or is absent wherein the peptide is labeled with a detectable marker.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing chemical groups, or amino acid sequences. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., complete or partial structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, method of making the claimed invention, level of skill and knowledge in the art and predictability in the art

sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for a genus of compound, polypeptide and peptidomimetic mentioned above longer than longer than 7 amino acid residues for treating or preventing any diseases, any disease such as any and all autoimmune diseases, any diseases such as cancer.

At the time of filing, the specification discloses only peptide consisting of six or seven amino acid residues in length selected from the group consisting of SEQ ID NO: 1-10 or the specific peptide listed in Table I and II that inhibits the binding of monoclonal CD23 antibody to CD23 expressing cell *in vitro* or inhibits iNOS production. The specification discloses the N-terminus of the peptide HENWPS (SEQ ID NO: 7) is acylated or the C-terminus of the peptide is amidated. The specification discloses only one retroinverted peptide of HENWPS, which is SPWNEH. However, only the non-retroinverted peptides of SEQ ID NO: 1-7 inhibits iNOS production as shown in Table 2. The specification further discloses administering peptide FHENWPS (p30A) of SEQ ID NO: 1 inhibited the production of TNF and ameliorated the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

As of the filing date of instant application, Applicants are not in possession of any compound or polypeptide other than the specific peptides consisting of the amino acid sequence of SEQ ID NO 1-10 or the peptide listed in Table 1 and 2. There is a lack of disclosure about the structure of any compound, any peptidomimetics or any polypeptide longer than 6 or 7 amino acid residues. The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends. There is no disclosure as to which amino acids to be added,

such that the compound comprising a peptide having a combination of amino acid residues still maintains binding to CD23 of at least about 10^{-6} M.

With respect polypeptide comprising the peptide of claim 1 wherein said polypeptide comprises from about 6 to about 100 amino acids (claim 10) or from about 6 to about 70 amino acids (claim 11), there is not a single polypeptide longer than 7 amino acid residues in the specification as filed. As such, the rest of 93 amino acid residues or 63 residues, respectively in the polypeptide are not disclosed.

Stryer et al (in Biochemistry, Third edition, W H Freeman Company, New York, pages 31-33, 1998; PTO 892). teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a protein having the same biological activity are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Ngo et al (The Protein Folding Problem and Tertiary Structure Prediction, pp. 491-495, 1994; PTO 892) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 with an expectation of obtaining a derivative maintaining the same biological activity.

At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the specification discloses substituting even a single amino acid in the peptide of SEQ ID NO: 1 from P to A resulted in lost of inhibition of iNOS production from 74% to 26%, see specification at page 28, Table II compound 328, in particular.

With respect to any peptidomimetic of claim 1, the specification discloses only the peptide of SEQ ID NO: 1 wherein the amino acids are either D-isomer, the N-terminus of the peptide is either acylated or acetylated or the C-terminus is amidated, see Table 1. The specification does not teach substituting any amino acids, deleting, adding and/or a combination thereof in the peptide of SEQ ID NO: 1 still retain binding to CD23, other than the ones disclosed in Table I.

The specification at page 8 defines "peptidomimetic" is a compound that mimics the 'biological activity of a peptide but is no longer peptidic in chemical nature. A peptidomimetic is a compound that may no longer contain any peptide bonds (that is, amide bonds between amino acids). The term peptidomimetic as used herein includes within its meaning compounds that are no longer completely peptidic in nature, such as pseudo-peptides, semi-peptides and peptoids. Whether completely or partially non-peptide, peptidomimetics according to this invention provide a spatial arrangement of reactive chemical moieties that closely resembles the three-dimensional arrangement of active groups in the peptide on which, the peptidomimetic is based. As a result of this similar active-site geometry, the peptidomimetic has effects on biological systems which are similar to the biological activity of the peptide. The present invention encompasses peptidomimetic compositions which are analogs that mimic the activity of biologically active peptides according to the invention, i.e., the peptidomimetics are capable of binding to CD23.

However, the specification does not provide specific guidance regarding the chemical structure associated with the biological function or any specific *in vivo* use for the claimed peptidomimetics that are chemical in nature.

With respect to a pharmaceutical composition comprising any compound, any polypeptide or any peptidomimetic, the specification discloses administering only one peptide (p30A) consisting of the amino acid sequence FHENWPS (SEQ ID NO: 1) that inhibits the production of TNF and ameliorate the arthritis symptoms in in-bred Lewis rat induced mycobacterium butyricum (adjuvant induced model of arthritis).

However, the specification does not disclose administering any compound, any polypeptide comprising any peptide sequence as set forth in claims 1, 10-12, 21 or any peptidomimetic thereof is effective for treating a genus of diseases, much less preventing any and all diseases, any diseases such as any autoimmune diseases, other than SEQ ID NO: 1 for treating arthritis.

The state of the art at the time of filing is such that not all autoimmune diseases can be prevented. Further, Van Noort et al (International Review of Cytology 178: 127-205, 1998; PTO 892) teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). Because of the therapeutic indices of compound, protein or peptide can be species- and model-dependent, it is not clear that reliance on the use of adjuvant induced arthritis rat model and one species of peptide (SEQ ID NO: 1) accurately reflects the relative efficacy of treating all diseases by administering any compound, any polypeptide or any peptidomimetic, much less preventing any and all autoimmune diseases.

Because the described species of SEQ ID NO: 1 for treating arthritis is not representative of the entire claimed genus of peptides, compounds and peptidomimetics for treating a genus of diseases or autoimmune diseases , and the specification does not disclose the structural features shared by members of the genus of compounds, polypeptide longer than 7 amino acids in length and peptidomimetic that are not peptide in nature, one of skill in the art would conclude that applicant was not in procession of the claimed genus as a whole at the time of filing. Therefore, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 1-14, 21, 32, 35-36, 40-41, 49, 51 and 56.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115). Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1-3, 10-14, 21, 51 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449).

Jouault et al teach a compound such as KLH coupled to a peptide comprises the amino acid sequence FHENWPS where X1 is Phe (F), X2 is His (H), X3 is Glu (E), X4 is Asn (N), X5

is Trp (W), X6 is Pro (P) and X8 is absent (see page 695, col. 1, page 696, Table 1, in particular). The reference peptide FHENWPS has identical amino acids to the claimed CD23-binding peptide FHENWP of SEQ ID NO: 1 or p30A in Table 2. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The reference peptide is about 7 amino acids which is within the claimed polypeptide from about 6 to about 15, about 6 to 70 or about 6 to 100 amino acids. The reference further teaches a composition comprising the reference compound such as KLH coupled FHENWPS and a pharmaceutically acceptable carrier such as complete Freund's adjuvant (see page 699, col. 2, first full paragraph, in particular). Claim 40 is included in this rejection because the reference peptide FHENWPS inherently binds to CD23 of at least about 10^{-6}M. Thus, the reference teachings anticipate the claimed invention.

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1, 7, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449) in view of US Pat No 5,028,592 (issued July 2, 1991; PTO 892).

The teachings of Jouault et al have been discussed supra. Jouault et al further teaches the peptide is useful for making antibody.

The invention in claim 7 al differs from the teachings of the reference only in that the peptide wherein the N-terminus is acylated.

The invention in claim 8 al differs from the teachings of the reference only in that the peptide wherein the N-terminus is acetylated.

The invention in claim 9 al differs from the teachings of the reference only in that the peptide wherein the C-terminus is amidated.

The '592 patent teaches protective groups such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of a bioactive peptide reduce the susceptibility of the peptide to acid or enzymatic hydrolysis (see col. 4, lines 50-66, in particular). The '592 patent teaches protected peptides are more active pharmacologically than the unprotected peptide (see col. 4, lines 65-66, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the protective groups such as acyl or acetyl group bound to the amino terminus or the amidated group to the C-terminus of the '592 patent in the peptide comprises the amino acid sequence FHENWPS as taught by Jouault et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do so because the protective groups would the susceptibility of the peptide to acid or enzymatic hydrolysis and the protected peptides are more active pharmacologically than the unprotected peptide as taught by the '592 patent (see col. 4, lines 50-66, in particular). Jouault et al further teaches the peptide is useful for making antibody. One having ordinary skill in the art would have been motivated to use known technique to improve peptide known in the art as taught by the '592 patent to improve the peptide from enzymatic hydrolysis as taught by Jouault et al.

Given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007)* and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated recently into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

A) Combining prior art elements according known methods to yield predictable results.

B) Use of known technique to improve similar products in the same way.

C) "Obvious to try" --- choosing form a finite number of identified, predictable solutions, with a reasonable expectation of success.

D) Some teachings, suggestion, or motivation in the prior art that would lead to one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

Since reducing enzymatic hydrolysis or peptide in vivo is desirable and have been predictable at the time the invention was made, there would have been reasonable expectation of success in combine the references teachings to arrive at the claimed invention. An obviousness is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR International Co. V. Teleflex Inc. 82 USPQ2d 1385 (2007).* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

21. Claims 1, 35-36 and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449) in view of Heck et al (Proc Natl Acad Sci 93:4036-4039, April 1996; PTO 892).

The teachings of Jouault et al have been discussed supra.

The invention in claim 35 differs from the teachings of the reference only in that the peptide is a peptidomimetic of SEQ ID NO: 1 comprising at least one amino acid which is a D-isomer instead of naturally occurring L-isomer.

The invention in claim 49 differs from the teachings of the reference only in the peptidomimetic of SEQ ID NO: 1 is further labeled with a detectable marker.

Heck et al teach in recent years, a growing number of synthetic peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinectic profile) of the bioactive peptides (see page 4039, col. 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to improve the stability of the peptide of Jouault et al by substituting the natural occurring L-amino acid in the peptide of Jouault et al for the D-amino acid isomer as taught by Heck et al.

One having ordinary skill in the art would have been motivated to do so because Heck et al teach it is conventional at the time the invention was made to synthesize peptides containing D-amino acids to capitalize on the residues' ability to provide improved protease stability (pharmacokinectic profile), alter tertiary structure and affect activity of the bioactive peptides (see page 4039, col. 2, in particular). Claim 40 is included in this rejection because products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

22. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jouault et al (Glycobiology 11(8): 693-701, 2001; PTO 1449) in view of Heck et al (Proc Natl Acad Sci 93:4036-4039, April 1996; PTO 892) as applied to claims 1, 35-36 and 40-41 mentioned above and further in view of Harlow et al, in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, page 321-323, PTO 892).

The combined teachings of Jouault et al and Heck et al have been discussed supra. Jouault et al teach the reference peptide mimic epitopes corresponding to small oligomanosides or sugar sequence is highly specific and depends on the spatial structure presented by the sugar, see page 698, col. 1, in particular). Jouault et al further teaches labeled antibody such as HRP-labeled goat anti-Ig for detection assays (see page 698, col. 2, last paragraph, in particular).

The invention in claim 49 differs from the teachings of the reference only in the peptidomimetic of SEQ ID NO: 1 is further labeled with a detectable marker.

Harlow *et al* teach a method of labeling antibody or antigen (peptide) for a wide range of immunological assays and the advantage of enzyme label such as HRP is the shelf life, high sensitivity, and direct visualization is possible, see page 321-322, Table 9.1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to label the peptide of SEQ ID NO: 1 containing at least one D-amino acid of the Heck et al and Jouault et al with a detectable label such as Horse radish peroxidase (HRP) for detection or competition assay as taught by Jouault et al or Harlow et al.

One having ordinary skill in the art would have been motivated to label the peptide with any detectable marker such as HRP because the advantage of enzyme label such as HRP is the long shelf life, high sensitivity, and direct visualization is possible as taught by Harlow et al, see

page 321-322, Table 9.1, in particular). One having ordinary skill in the art would have been motivated to label the peptide to see if the peptide still binds to the sugar sequence because Jouault et al teach the reference peptide of SEQ ID NO: 1 is a mimic epitope corresponding to small oligomanosides or sugar sequence that is highly specific and depends on the spatial structure presented by the sugar, see page 698, col. 1, in particular).

23. The prior art of record and not relied upon is considered pertinent to applicant's disclosure.

JP2002187899 (published July 5, 2002 PTO 1449) a peptide such as Phe-His-Glu-Asn-Trp-Pro-Ser (V) which is 100% identical to the claimed SEQ ID NO: 1 and is relevant to the structure of the claimed invention claimed in the instant application, see pages 2-5, reference SEQ ID NO: 5, in particular.

DE 19749277 A1 (published May 5, 1999; PTO 1449) teaches a peptide such as Phe-His-Glu-Asn-Trp-Pro-Ser which is 100% identical to the claimed SEQ ID NO: 1 and is relevant to the structure of the claimed invention claimed in the instant application, see abstract, col. 2, lines 24-25, in particular.

Santamaria et al (Clinical Immunology 101(3): 296-302, 2001 teaches a peptide such as Phe-His-Glu-Asn-Trp-Pro-Ser which is 100% identical to the claimed SEQ ID NO: 1 and is relevant to the structure of the claimed invention claimed in the instant application, see page 298, col. 2, in particular.

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

26. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
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